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Polymicrobial Septicemia After Liver Biopsy

VINOD K. DHAWAN, MD, FRCP(C)
HARAGOPAL THADEPALLI, MD
DAVID D. ULMER, MD
ABBASI AKHTAR, MD, MRCP
Los Angeles

NEEDLE BIOPSY of the liver engenders minimal risk to patients when the procedure is expertly done. In Lindner's series of 123,000 biopsies, the death and morbidity rates were only 0.015% and 0.29%, respectively.¹ Although a variety of complications may follow liver biopsy,^{2,3} serious infection rarely occurs. We report an unusual case of polymicrobial septicemia after percutaneous liver biopsy and summarize the pertinent literature.

Report of a Case

A 73-year-old man was admitted to Martin Luther King, Jr/Charles R. Drew Medical Center (Los Angeles) because of yellow eyes and dark urine for two months and pruritus for two weeks. He had no nausea, vomiting, abdominal pain, fever or recent weight change. There was no history of alcohol abuse, exposure to hepatotoxins, previous hepatitis or blood transfusion. He had undergone a cholecystectomy ten years before. On physical examination he appeared comfortable and had normal temperature and blood pressure. The liver span on percussion was 15 cm and the edge was firm, smooth and slightly tender. There were no other abnormal findings.

Laboratory studies at the time of admission gave the following values: hemoglobin, 12.5 grams per dl; hematocrit, 38.6%; leukocyte count, 9,600 per μ l, with

normal differential, and platelet count, 216,000 per μ l. The urine contained bile. The serum glucose, blood urea nitrogen, electrolytes and amylase levels were normal. The total bilirubin was 4.6 mg per dl (direct, 2.4 mg per dl); serum aspartate amino transferase (AST, or SGOT), 212 IU (normal 8 to 30); serum alanine amino transferase (ALT, or SGPT), 348 IU (normal 3 to 36); alkaline phosphatase, 216 IU per liter (normal 25 to 97); total protein, 6.5 grams per dl; albumin, 3.5 grams per dl; prothrombin time, 10.4 seconds (control 10.4), and partial thromboplastin time, 27 seconds (control 31). Tests for hepatitis B surface antigen, surface antibody and core antibody were negative, as were those for hepatitis A antibody and antinuclear antibody. Results of chest and abdominal roentgenograms, abdominal ultrasound, a liver-spleen scan with technetium Tc 99m and an electrocardiogram were normal.

Because of a question of intrahepatic cholestasis, a liver biopsy was done on the fourth hospital day using a TruCut needle. The biopsy needle was inserted through the right eighth intercostal space in the mid-clavicular line and two passes were made into the liver. The liver biopsy specimen showed inflammation of portal tracts with adjacent necrosis and bile cholestasis, suggesting mild chronic hepatitis. About eight hours later, the patient had a shaking chill and his temperature rose to 39°C (102.4°F). The leukocyte count was 14,600 per μ l with a leftward shift. Results of urine analysis, urine culture and chest x-ray study were all normal. However, the following two Gram-negative bacilli were cultured from the blood: *Klebsiella oxytoca*, sensitive to gentamicin, tobramycin, amikacin, cephalothin, cefoxitin, chloramphenicol and trimethoprim-sulfamethoxazole but resistant to ampicillin, carbenicillin and tetracycline; and *Escherichia coli*, sensitive to all aforementioned antibiotics.

Therapy with gentamicin sulfate, 80 mg given intravenously every eight hours, was started on the sixth hospital day. The patient's temperature continued to rise to 38°C to 39°C (101°F to 103°F) each day. Repeat laboratory studies showed a total bilirubin of

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From the Divisions of Infectious Diseases and Gastroenterology, Department of Medicine, Charles R. Drew Postgraduate Medical School and UCLA School of Medicine, Los Angeles.

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Reprint requests to Vinod K. Dhawan, MD, King/Drew Medical Center, 12021 S Wilmington Ave, Los Angeles, CA 90059.

19 mg per dl (direct, 8.8 mg per dl); AST, 41 IU; ALT, 111 IU, and alkaline phosphatase, 805 IU per liter. Findings of an abdominal ultrasound examination on the ninth hospital day were again normal. Hepatobiliary imaging with technetium Tc 99m diisopropyl iminodiacetic acid on the same day, however, showed possible narrowing of the common bile duct. A blood culture obtained on the tenth hospital day again showed *E coli* with unchanged antibiotic sensitivities. Cefoxitin sodium, 2 grams intravenously every six hours, was administered along with gentamicin. A body scan using gallium citrate Ga 67 showed no unusual uptake.

On the 14th hospital day an exploratory laparotomy was done. A collection of about 20 ml of hemorrhagic fluid was noted under the capsule of the liver at the site of the liver biopsy but the rest of the liver surface appeared normal. The fluid was sterile to culture. Results of an intraoperative cholangiogram ruled out biliary obstruction. A wedge biopsy specimen of the liver again showed mild chronic hepatitis. The post-operative course was uneventful and the patient remained afebrile. He continued to receive cefoxitin and gentamicin for 14 additional days, his jaundice slowly decreased and he improved progressively. Blood cultures on the 16th hospital day and subsequently were negative. The patient was discharged well on the 31st hospital day and was asymptomatic at the time of follow-up a month later.

Discussion

The liver, containing about 60% of the entire reticuloendothelial system, plays a major role in defense against bacterial invasion and sequesters bowel organisms with high efficiency.⁴ Whereas bacteria can

be cultured from the portal vein at operation in up to a third of patients, peripheral blood specimens cultured simultaneously are uniformly sterile.⁵ In cirrhosis, spontaneous bacteremia may occur due to altered structure and blood flow.⁶

Despite the fact that hepatic macrophages often contain bowel organisms, infections complicating needle biopsy are remarkably rare. Transient bacteremia consequent to this procedure, however, does occur with some frequency. Le Frock and co-workers, who obtained blood cultures from 89 patients before and 5, 10, 15 and 30 minutes after liver biopsy,⁷ found transient bacteremia in 12 (13.5%). The organisms cultured included *E coli*, *Klebsiella*, *Bacteroides*, *Enterococcus*, *Diphtheroides*, *Staphylococcus aureus*, α -hemolytic streptococcus and *Streptococcus pneumoniae*. In five of these patients, the same organism was found in blood and in the liver biopsy material, supporting the view that bacteria from the liver entered the bloodstream. Notably, all patients remained symptomatic. Other investigators have also found transient bacteremia after liver biopsy but with lesser frequency and usually involving patients compromised by hepatitis and receiving immunosuppressive therapy.⁸⁻¹⁰

Although bacteremia after liver biopsy is not infrequent, septicemia is distinctly unusual. Reported cases are summarized in Table 1. All patients were 58 years or older and all except one were men. Causative organisms mirror the bowel flora, with *E coli* being the most frequent offender. *K oxytoca* septicemia following liver biopsy is reported for the first time in the present case.

There are only two previous reports of polymicrobial septicemia following liver biopsy. In one (case 1

TABLE 1.—Report of 8 Cases of Septicemia Following Liver Biopsy*

Case, Age, Sex	Liver Biopsy Diagnosis	Causative Organisms	Type of Needle	Therapy	Outcome	Reference
1 68 ♂ ..	Subacute pericholangitis	<i>Escherichia coli</i> and <i>Streptococcus viridans</i>	Not reported	Penicillin and gentamicin; refused surgical procedure	Improved; lost to follow-up	LoIudice et al ¹¹
2 79 ♂ ..	Chronic cholangitis with secondary biliary cirrhosis	<i>E coli</i>	Not reported	Ampicillin; cholecystectomy	Resolved	LoIudice et al ¹¹
3 58 ♂ ..	Cirrhosis and carcinoma of liver	<i>E coli</i>	Not reported	Gentamicin	Died; had right subdiaphragmatic abscess	LoIudice et al ¹¹
4 79 ♀ ..	Normal liver	<i>E coli</i>	Menghini	Gentamicin, then ampicillin	Resolved	Murray and Dugowson ¹²
5 58 ♂ ..	Chronic cholangitis	<i>E coli</i>	TruCut	Gentamicin; operation to remove villous adenoma of ampulla of Vater	Resolved	Navarro et al ¹³
6 58 ♂ ..	Typhoid hepatitis	<i>Salmonella</i>	Menghini	Chloramphenicol	Resolved	Singh et al ¹⁴
7 68 ♂ ..	Portal fibrosis, chronic cholangitis	<i>E coli</i> and <i>Bacteroides fragilis</i>	Vim-Silverman	Ampicillin and gentamicin, then changed to cefazolin and gentamicin and chlorphenicol; refused surgical procedure	Resolved	Moreira Vicente et al ¹⁵
8 73 ♂ ..	Chronic hepatitis	<i>E coli</i> and <i>Klebsiella oxytoca</i>	TruCut	Gentamicin and cefoxitin	Resolved	Present case

*Another case of possible septicemia involving *Clostridium welchii* (*Clostridium perfringens*) was reported but no details were given (Morris et al¹⁶).

in the table), *E coli* and *Streptococcus viridans* were found¹¹ and in the other (case 7) *E coli* and *Bacteroides fragilis*.¹⁵ In the latter, a small intestinal perforation could not be excluded, a condition not evident in our case.

With the exception of one patient (case 4), all previously reported cases had an identifiable source of septicemia such as subdiaphragmatic abscess or cholecystitis. In our patient no such foci of infection were identifiable; hence, this constitutes the second report of a de novo septicemia following liver biopsy and the first such instance of polymicrobial infection.

The abrupt onset of fever, chills and leukocytosis within eight hours of the biopsy strongly suggested an infectious process in our patient. Because strict asepsis was observed during the procedure and no other source of infection was discerned after a meticulous search, including laparotomy, we speculate that bacteria sequestered in hepatic macrophages were introduced into the bloodstream by the biopsy. A complex interaction of a subcapsular hematoma, microorganisms and the host defenses then favored the development of septicemia.

Two cases of serious infection other than septicemia following liver biopsy have been reported. Klein and associates reported the development of a liver abscess in a 47-year-old man who had undergone liver biopsy with a Menghini needle a month before.¹⁷ Schnyder and colleagues reported peritonitis occurring after needle biopsy of the liver in a patient who had a liver abscess.¹⁸

The development of fever shortly after a liver biopsy should suggest the possibility of septicemia and therapy should be initiated promptly. Because the vast majority of organisms causing sepsis under this circumstance are coliform aerobic bacilli, antibiotic therapy should be directed empirically against such bacteria. Use of an aminoglycoside with a cephalosporin would appear most appropriate until the reports of blood culture become available. Prognosis appears to be ex-

cellent in most cases. A surgical procedure should be done to relieve biliary obstruction if present.

Because transient bacteremia after liver biopsy is not unusual, the question arises as to the need for antibiotic prophylaxis for patients with structural abnormalities of the heart valves and vascular prostheses. No objective data are available to answer this question. However, because bacteremia following liver biopsy is most commonly due to aerobic Gram-negative bacilli and because these organisms are infrequent causes of endocarditis, routine use of toxic agents such as aminoglycosides are not warranted.

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